spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of said structural conformations being indicative of the effect of said enzyme peptide on said peptide substrate.

52. The composition of claim 51, wherein said semi-synthetic multiple labeled polypeptide is said peptide substrate.

53. The composition of claim 51, wherein said semi-synthetic multiple labeled polypeptide is said active enzyme peptide.

C15 cont.

54. The composition of claim 51, wherein said active enzyme peptide is a kinase.

55. The composition of claim 54, wherein said kinase is Abelson protein tyrosine kinase.

56. The composition of claim 52, wherein said peptide substrate is Crk-II.

57. The composition of claim 51, wherein said modification of at least one substrate amino acid is a post-translational modification.

58. The composition of claim 57, wherein said modification of at least one substrate amino acid is a phosphorylation modification.

59. The composition of claim 57, wherein said

modification of at least one substrate amino acid is a dephosphorylation modification.

60. The composition of claim 51, further comprising a modulator of said active enzyme peptide.

61. The composition of claim 60, wherein said modulator of said active enzyme peptide inhibits said enzyme activity.

62. The composition of claim 60, wherein said modulator of said active enzyme peptide promotes said enzyme activity.

63. The composition of claim 51 wherein one of said detectable proximity-sensor peptides is at the N-terminus of said semi-synthetic multiple labeled polypeptide and the other of said detectable proximity-sensor peptides is at the C-terminus of said semi-synthetic multiple labeled polypeptide.

C45 cont.

64. The composition of claim 51 wherein said active enzyme peptide is produced recombinantly.

65. The composition of claim 51 wherein said active enzyme peptide further includes an N-terminal cysteine and a C-terminal $^{\alpha}$thioester.

66. The composition of claim 51 wherein said first and second detectable proximity-sensor peptides of said semi-synthetic multiple labeled polypeptide comprise a FRET pair.

67. The composition of claim 66 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY fluorescein and BODIPY FL fluorescein, β-phycoerythrin and CY5, and pyrene and coumarin.

68. The composition of claim 67, wherein said FRET pair comprises fluorescein and tetramethylrhodamine.

69. The composition of claim 51 wherein said detectable proximity-sensor peptide is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

70. The composition of claim 51 having the sequence of SEQ ID NO: 8.

71. The composition of claim 51, wherein said semi-synthetic multiple labeled polypeptide comprises a third detectable proximity-sensor peptide incorporated into a third position of said semi-synthetic multiple labeled polypeptide.

C45 cont.

72. A composition for detecting the effect of a kinase on a substrate, comprising an active kinase peptide which acts on a peptide substrate, said kinase activity producing a phosphorylation of at least one substrate amino acid, and a peptide substrate for said enzyme, wherein at least one, but not both of said active kinase peptide and said peptide substrate comprises at least a first detectable proximity-sensor peptide incorporated into a first position of one of said peptides and a second detectable proximity-sensor peptide incorporated into a second position of said one peptide, thereby providing a semi-synthetic multiple labeled polypeptide, wherein said semi-synthetic multiple labeled polypeptide has a first structural conformation in an unmodified state and a second structural conformation in a modified state, said proximity sensors being spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of

said structural conformations being indicative of the effect of said active kinase peptide on said peptide substrate.

73. The composition of claim 72, wherein said kinase is Abelson protein tyrosine kinase.

74. The composition of claim 72, wherein said substrate is Crk-II.

75. A composition for detecting the effect of an enzyme on a substrate, comprising an active enzyme peptide which acts on a peptide substrate, said enzyme activity producing a modification of at least one substrate amino acid, said substrate remaining intact, and a peptide substrate for said enzyme, wherein both of said active enzyme peptide and said peptide substrate comprise at least a first detectable proximity-sensor peptide incorporated into a first position of one of said peptides and a second detectable proximity-sensor peptide incorporated into a second position of one of said peptides, thereby providing two preselected polypeptides having at least two sensor peptides, wherein said preselected polypeptides having at least two sensor peptides have a first structural conformation in an unmodified state and a second structural conformation in a modified state, said proximity sensors being spaced apart in said first structural conformation at a distance which is characteristic of said unmodified state and being spaced apart in said second structural conformation at a distance which is characteristic of said modified state, detection of one of said structural conformations being indicative of the effect of said enzyme peptide on said peptide substrate.

G5 cont.

76. The composition of claim 51, wherein said detectable proximity-sensor peptide is a small molecule fluorophore.